UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/775,169	02/11/2004	Michael E. Burczynski	WYE-024	1858

54623 7590 04/04/2007

KIRKPATRICK & LOCKHART PRESTON GATES ELLIS LLP
STATE STREET FINANCIAL CENTER
ONE LINCOLN STREET
BOSTON, MA 02111-2950

EXAMINER	
SCHLAPKOHL, WALTER	
ART UNIT	PAPER NUMBER
1636	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/775,169	BURCZYNSKI ET AL.	
	Examiner	Art Unit	
	Walter Schlapkohl	1636	wal

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *6,13 and 18-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 7-12 and 14-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/15/2005 and 9/15/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of the papers filed 1/3/2007. Claims 1-20 are pending. Claims 6, 13 and 18-20 are withdrawn. Claims 1-5, 7-12 and 14-17 are under examination in the instant Office action.

Election/Restrictions

Applicant's election with traverse of Group I in the reply filed on 1/3/2007 is acknowledged. Applicant traversed "the nonallowance of the linking claims of group I and II" (see Remarks filed 1/3/07). This is not found persuasive because the requirement for election/restriction mailed 7/13/2006 indicated that "[t]he restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claim 1" (see page 8, 3rd full paragraph; emphasis added). The restriction requirement did not evaluate the patentability or render any judgment on the linking claim's allowability or nonallowability.

The requirement is still deemed proper and is therefore made FINAL.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
It does not identify the citizenship of each inventor.

Claim Objections

Claims 4 and 9 are objected to because of the following informalities:

Claim 4 recites "[t]he method according to claim 3, wherein the solid tumor is RCC" in line 1 (emphasis added). Claim 4 is objected to because the acronym RCC should be spelled out at its first occurrence in the claims.

Claim 9 recites "[t]he method according to claim 1, wherein the expression profile is determined by RT-PCR or immunoassays" in lines 1-2 (emphasis added). Claim 9 is objected to because the acronym RT-PCR should be spelled out at its first occurrence in the claims.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 7-10, 12 & 14-16, and therefore dependent claims 4-5 & 11, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Claim 1 recites "[a] method comprising comparing an expression profile of at least one gene in a peripheral blood sample of a patient to a reference expression profile of said at least one gene, wherein said at least one gene is differentially expressed in peripheral blood mononuclear cells (PBMCs) of patients who have a non-blood disease and are subject to a drug therapy as compared to PBMCs isolated from said patients before said drug therapy, and wherein the patient has the non-blood disease and is being treated by said drug therapy" in lines 1-6 (emphasis added).

Claim 1 is vague and indefinite in that the metes and bounds of a "non-blood disease" are unclear. Does Applicant intend any disease which is not characterized by a blood

disorder, i.e., not sickle cell anemia or stroke; or does Applicant intend some other set of diseases?

Similarly, claims 3, 12 and 17 recite the term "non-blood disease." Claims 3, 12 and 17 are vague and indefinite as explained for claim 1, above.

Claim 1 is also vague and indefinite in that it is not clear how the phrase "and wherein the patient has the non-blood disease and is being treated by said drug therapy" in line 6 modifies the claim. Is Applicant intending to further limit the patients encompassed within the scope of those whose expression profiles will be compared to a reference expression profile, or is Applicant intending to further limit the patients from which said at least one gene is differentially expressed?

Claim 2 recites "[t]he method according to claim 1, wherein said drug therapy is a CCI-779 therapy" in lines 1-2 (emphasis added). Claim 2 is vague and indefinite in that the metes and bounds of a "CCI-779 therapy" are unclear. Does Applicant intend any therapy which comprises the administration of CCI-779 alone or in combination with other drugs to a patient, or does Applicant intend a treatment which comprises a particular dose and schedule for CCI-779 administration alone?

Similarly, claim 15 recites a "CCI-779 therapy" in lines 1-2. Claim 15 is vague and indefinite as explained for claim 2, above.

Claim 8 recites "[t]he method according to claim 1, wherein the peripheral blood sample comprises enriched PBMCs" in lines 1-2 (emphasis added). Claim 8 is vague and indefinite in that the metes and bounds of a sample comprising "enriched PBMCs" are unclear. The specification teaches that "[b]y 'enriched,' it means that the percentage of PBMCs in the sample is higher than that in whole blood" (see page 7, paragraph [0027]). Whose whole blood is intended? Must the higher percentage of PBMCs be enriched prior to taking the whole blood sample from the patient? In other words, must the PBMCs be naturally enriched as compared to the whole blood of another patient, or can a peripheral blood sample simply comprise enriched PBMCs after centrifugation?

Claim 9 recites "[t]he method according to claim 1, wherein the expression profile is determined by RT-PCR or immunoassays" in lines 1-2 (emphasis added). Claim 9 is unclear because "the expression profile" in line 1 lacks clear and positive antecedent basis. Does Applicant intend the "first" expression profile of at least one gene, the reference expression profile, or both?

Claim 10 recites "[t]he method according to claim 1, wherein the reference expression profile is an average expression profile of said at least one gene in peripheral blood samples isolated from said patients before said drug therapy" in lines 1-3 (emphasis added). Claim 10 is vague and indefinite in that the metes and bounds of an "average expression profile" are unclear. Does Applicant intend such a method wherein the expression levels of said at least one gene are measured and averaged, or does Applicant intend such a method wherein the reference expression profile represents a "typical" expression level for said gene from said patient before treatment?

Claim 12 recites "[t]he method according to claim 1, wherein said at least one gene includes one or more genes which are over-expressed or under-expressed in PBMCs of patients who have the non-blood disease as compared to PBMCs of humans who do not have the non-blood disease, and wherein said drug therapy is capable of down-regulating or up-regulating expression of said one or more genes in PBMCs of patients who have the non-blood disease" in lines 1-6 (emphasis added). Claim 12 is vague and indefinite in that the metes and bounds of genes which are either "over-expressed" or "under-expressed" as compared to said genes in PBMC of humans who do not have the non-blood disease are unclear. Does Applicant intend genes with any level of

expression that is greater than that found in PBMCs of any human who does not have the non-blood disease, or does Applicant intend that an "over-expressed" gene must surpass a certain threshold of expression in the comparison? Furthermore, does Applicant intend to use genes which are over- or under-expressed in patients before treatment with said drug therapy or after treatment in said drug therapy?

Claim 14 recites "[t]he method according to claim 1, wherein RNA transcripts of said at least one gene are capable of hybridizing under stringent or nucleic acid array hybridization conditions to one or more qualifiers selected from the Qualifier Table" in lines 1-4 (emphasis added). Claim 14 is vague and indefinite in that the metes and bounds of "nucleic acid array hybridization conditions" and the metes and bounds of "stringent" conditions are unclear.

The specification teaches:

> Labeled probes were denatured at 99°C for 5 minutes and then 45°C for 5 minutes, and hybridized to oligonucleotide arrays comprised of over 12,500 human gene probes (HgU95A, Affymetrix). Arrays were hybridized for 16 hours at 45°C. The hybridization buffer was comprised of 100 mM MES, 1 M [Na+], 20 MM EDTA, and 0.01% Tween 20. After hybridization, the cartridges were washed extensively with non-stringent wash buffer (6 x SSPET), such as three 1.0-minute washes at room temperature. These hybridization and wash conditions are herein collectively referred to as "nucleic acid array hybridization conditions.

(page 129, paragraph [0461]; emphasis added). Because the specification does not clearly define the wash conditions encompassed by "nucleic acid array hybridization conditions," the metes and bounds of "nucleic acid array hybridization conditions" are unclear. For example, is 1 wash for 1 minute with 6X SSPET encompassed?

Similarly, the specification teaches at page 119, paragraph [0423], that "[a]s used herein, 'stringent conditions' are at least as stringent as, for example, conditions G-L shown in Table 7." Because the specification does not clearly define the wash conditions encompassed as "stringent" and because stringent is a relative term, and further because one of ordinary skill in the art would not be reasonably apprised of the scope of the invention, the claim is vague and indefinite.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 7-12 and 14-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art, the amount of experimentation necessary and the relative skill levels of those in the art. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the Invention and Breadth of the Claims: The claims are drawn to methods comprising a comparison between an expression profile from at least one gene in a peripheral blood sample of patient who has a non-blood disease before and after treatment with a drug. While claim 5 is drawn to such a method comprising the use of profilin-1, the rest of the claims encompass the use of any gene or set of genes from peripheral blood mononuclear cells (PBMCs) to detect any gene which can be modulated by the drug therapy. The claims also encompass and non-blood disease and any drug treatment. The nature of the invention is complex in that gene expression patterns involving potentially thousands of different genes are involved.

Furthermore, the PBMCs from which the expression patterns will be obtained are not themselves diseased and are only presumed to comprise genes which can be modulated by the drug therapy in a way that is indicative of a "drug activity gene." Thus, the invention is broad in scope and very complex.

Guidance Provided by the Specification and the Existence of Working Examples: The specification teaches that the invention employs PBMCs "as surrogate tissues for the detection of *in vivo* activities of CCI-779 or other drugs" (see pages 1-2, paragraph [0004]). The specification further teaches that the invention employs systematic gene expression analysis to identify genes whose expression in peripheral blood can be modulated by a therapeutic agent such as CCI-779 (see page 5, paragraph [0019]). These "drug activity genes" can further be utilized such that changes in the peripheral blood expression profile of such genes are indicative of the *in vivo* activity of the drug therapy (page 4, [0017]). The specification discloses 36 CCI-779 activity genes so identified (see page 113-117, Table 6, paragraph [0415]).

On the whole, the disclosure appears to assert that, because differences in gene expression can be determined among genes expressed in PBMCs from a subject with a non-blood disease pre- and post-drug therapy, and because these genes can be

identified, differences in PBMC gene expression before and after drug treatment would be indicative of the *in vivo* effect of a drug therapy upon any given non-blood disease.

However, the specification does not provide a single working example of such a complex method, wherein the genes identified before and after drug therapy are indicative of the *in vivo* activity of the drug therapy utilized, especially with regard to the effect of the drug therapy upon the non-blood disease.

Nor does the specification teach how a difference in one gene's expression (be it profilin-1 or any other gene) should or could be measured such that the difference is indicative of CCI-779's activity or any other drug's activity on a non-blood disease.

The specification also does not teach any examples of a drug therapy other than the administration of CCI-779 for which the claimed method has been practiced.

State of the prior art and level of predictability in the art: The "predictability or lack thereof" in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention

pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art. Accordingly, what is known in the art provides evidence as to the question of predictability. The physiological art is recognized as unpredictable (MPEP 2164.03). As set forth in *In re Fischer*, 166 USPQ 18 (CCPA 1970), compliance with 35 USC §112, first paragraph requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. In cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resorting to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.

The question of predictability in the instant case has to do with whether the skilled artisan would be able to extrapolate from the disclosed CCI-779-modulated genes and the knowledge

available in the art regarding the correlated effects of drug therapy upon any non-blood disease and the simultaneous changes in PBMC gene expression, such that the skilled artisan could practice the claimed method to determine if changes in the PBMC expression profiles before and after drug treatment were indicative of the *in vivo* activity of the drug on the non-blood disease.

The claimed method proposes to use any "drug activity gene" as a biomarker or surrogate endpoint for efficacy in the treatment of any non-blood disease with any drug therapy. The art recognizes that before a putative biomarker can be used as a surrogate endpoint it must be validated as such. Wagner (*Dis. Markers* **18**(2):41-46, 2002) acknowledges in the Abstract, "Putative biomarkers are typically identified because of a relationship to known or hypothetical steps in a pathophysiologic cascade. Biomarker discovery can also be effected by expression profiling experiment using a variety of array technologies and related methods." However, Wagner cautions, "A rational basis for recommending the use of a putative biomarker does not guarantee the utility of the biomarker or its qualification as a surrogate endpoint" (paragraph bridging the left and right columns on page 43) and

"Biomarkers require validation in most circumstances" (paragraph bridging pages 43-44).

Frank *et al.* (*Nature Rev.* **2**:566-580, 2003) concurs, stating, "The standard concepts of test-re-test reliability and validity apply with equal force to clinical biomarkers as they do in any assay system" and, "The work required to establish the reliability and validity of a new biomarker should not be underestimated in general, and in particular needs of planning for each combination of clinical indication and mechanism of action" (paragraph bridging the left and right columns on page 568). Feng *et al.* (*Pharmacogenomics* **5**:709-719, 2004) teaches, "The development and validation of clinically useful biomarkers from high-dimensional genomic and proteomic information pose great research challenges. Present bottle necks include: that few of the biomarkers showing promise in initial discovery were found to warrant subsequent validation...A molecular profiling approach, although promising, has a high chance of yielding biased results and overfitted models" (Abstract).

Viewed as a whole, the art clearly teaches that the utility of a putative biomarker as a surrogate endpoint for any disease state is unpredictable and must be validated.

With regard to the use of biomarkers in renal cell carcinoma (RCC), an article published after Applicant's

effective filing date describes "disease-associated" expression profiles in peripheral blood mononuclear cells (PBMCs) from patients with advanced renal cell carcinoma (Twine *et al. Cancer Research* **63**(18):6069-6075, 2003). However, Twine et al do not disclose that such gene expression patterns can be used to detect RCC in a patient. Rather, Twine et al teach the presence of expressed, disease-associated genes in the PBMCs of RCC patients, which if additional experiments were to bear such findings out, could "represent the foundation on which to build disease-specific gene sets that can be used as part of a molecular diagnosis of disease using peripheral blood" (see page 6075, last paragraph, as well as page 6074, Figure 2). Twine *et al.* also teach that "it is currently unknown whether in the context of RCC or any other active solid tumor burden there exists correspondingly distinct markers of gene expression in the PBMCs of affected individuals" (page 6069, first column, first paragraph). Thus, even after Applicant's effective filing date the art does not recognize gene expression profiles from PBMCs which are necessarily diagnostic of renal cell carcinoma. It would therefore be an even larger hurdle to determine from among those putative biomarkers of RCC, those genes which could act as surrogates for the efficacy of a drug therapy upon RCC.

Thus, the state of the prior art with regard to the use of surrogate endpoints in general was underdeveloped and unpredictable at the time of Applicant's filing; the state of the art was silent with regard to the use of PBMC biomarkers to determine the efficacy of drug therapy on RCC in particular.

Amount of Experimentation Necessary: Given the underdeveloped state of the art and the level of unpredictability in the art, one of ordinary skill in the art would have been required to perform an undue amount of experimentation in order to first, accurately determine gene expression differences in PBMCs of patients with a non-blood disease before and after drug treatment. Then, once differences in gene expression were found (if any), one of ordinary skill in the art would have to determine which of those difference were indeed indicative of the drug therapy and could therefore be used as an indication of the drug's activity *in vivo*. The *in vivo* drug activity on PBMC gene expression and upon the non-blood disease would need to be correlated. This amount of experimentation is exacerbated by the large breadth of the claims, which would require one of ordinary skill in the art to determine which genes were associated before and after treatment with any drug for any non-blood disease.

"It must be remembered...that '[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. Tossing out the mere germ of an idea does not constitute enabling disclosure.' *Genentech*, 108 F.3d at 1366 (quoting *Brenner v. Manson*, 383 U.S. 519, 536 [148 USPQ 689] (1966) (stating, in context of the utility requirement, that 'a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion')). Thus, while the need for some experimentation is by no means necessarily fatal, 'reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.' Id." *University of Rochester v. G.D. Searle & Co.*, 68 USPQ2d 1424 at 1436 (W.D.N.Y. 2003).

Given no more that what is provided in the instant application and the relevant art, the skilled artisan would not know how to practice the claimed invention (i.e., which differences in gene expression to use in combination with which non-blood diseases and which drug therapies, etc.) such that the difference(s) in gene expression were indicative of the drug therapy's efficacy *in vivo*. Given the unpredictable nature of the invention and the expansive scope of the claims, the amount of experimentation would clearly be undue. Therefore, the

disclosure fails to adequately enable the claims and the claims are properly rejected under 35 U.S.C. §112, first paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 9, 10-11 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by DiPaola et al (*J. Clin. Oncol.* **17**(7):2213-2218, 1999; IDS Ref.).

DiPaola et al teach a method comprising comparing an expression profile of at least one gene (bcl-2) in a peripheral blood sample of a patient to a reference expression profile of said at least one gene, wherein said at least one gene is differentially expressed in peripheral blood mononuclear cells (PBMCs) of patients who have a non-blood disease, i.e., prostate cancer and/or tumors from other organs (see entire document, especially page 2213, the Abstract; page 2215, Table 1; and page 2217, Figure 3). DiPaola teach such a comparison wherein the expression profiles compared are of patients with the non-blood

disease, both before and after treatment with 13-cis-retinoic acid (CRA), IFNα and paclitaxel (TAX). With regard to claim 8, DiPaola et al teach such a method wherein the PBMCs were "enriched" insofar as the PBMCs were centrifuged in CPT mononuclear cell isolation tubes and "the mononuclear cell layer was removed" (see page 2214, 2nd column, 3rd paragraph). With regard to claim 9, DiPaola et al teach such a method wherein the expression profile is determined by immunoassay, i.e., Western blot (see page 2217, Figure 3 and page 2214, 2nd column, 3rd full paragraph). With regard to claim 10, DiPaola et al teach such a method wherein the bcl-2 expression profile is an "average" expression profile insofar as the expression profile represent the average expression level within the PBMCs of a given patient at a given time point.

It is noted that this Office action contains rejections of the same claims under 35 U.S.C. 112, 1st paragraph (enablement) and 35 U.S.C. 102(b). While these rejections may seem contradictory, they are not because each is based upon a different legal analysis, i.e. sufficiency of the disclosure of the instant application to support claims under 35 U.S.C. 112, 1st paragraph vs. sufficiency of a prior art disclosure to

anticipate or render obvious an embodiment of the claimed invention (See *In re Hafner*, 161 USPQ 783 (CCPA 1969)).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4 and 10-11 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 of copending Application No. 10/793,032. Although the conflicting claims are not identical,

the claims of the 10/793,032 application anticipate those of the instant application; i.e., the claims of the 10/793,032 application are drawn to methods comprising the comparison of an expression profile of at least one gene in a peripheral blood sample of a patient to a reference expression profile of said at least one gene, wherein said at least one gene is differentially expressed in peripheral blood mononuclear cells (PBMCs) of a patient who has the non-blood disease and who is being treated by a drug therapy as compared to PMBCs of said patient before said drug therapy. Furthermore, both sets of claims encompass embodiments wherein the drug therapy is CCI-779 therapy and wherein the non-blood disease is a solid tumor. Therefore, these claims anticipate claims 1-4 and 10-11 of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claim is allowed.

Certain papers related to this application may be submitted to the Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the

Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is (571) 273-8300. Note: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent applications to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at (800) 786-9199.

Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should be directed to Walter Schlapkohl whose telephone number is (571) 272-4439. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Joseph Woitach can be reached at (571) 272-0739.

Walter A. Schlapkohl, Ph.D.
Patent Examiner
Art Unit 1636

March 27, 2007

DANIEL M. SULLIVAN, PH.D.
PRIMARY EXAMINER